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**HUMAN RESOURCES**

**EFFECTS OF PYRIDOSTIGMINE BF.OMIDE ON  
A-10 PILOTS DURING EXECUTION OF  
A SIMULATED MISSION: PHYSIOLOGY**

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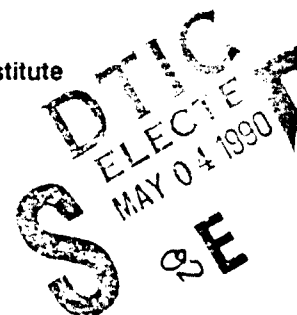
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13. ABSTRACT (Maximum 200 words) <p>— This report documents the physiological results of an experiment that was conducted to determine the effects of pyridostigmine bromide (PB) (30mg, three times per day) on pilot performance and physiology. Both sets of data were collected in an A-10 flight simulator with an Advanced Visual Technology System (AVTS). The subjects were 24 A-10 pilots who were trained on the following simulated tasks over three 55-minute sessions: takeoff, patterns, emergency procedure, and landing; air-to-air refueling; conventional low-angle strafing; and low-level ingress/RED FLAG. Next, during two test sessions, 48 hours apart, the pilots were tested using a double-blind procedure on the same tasks in a PB condition and in a placebo condition. In the two test sessions, 12 of the pilots wore the chemical defense ensemble (CDE) and the other 12 pilots wore standard flight gear (SFG). PB dosages led to reports of 27 symptoms among 12 (50%) of the pilots. Under the placebo condition, in contrast, only 5 (20%) of the pilots reported a total of 5 symptoms. Analyses of PB effects on physiological functions and on various biobehavioral measures showed suppression of heart rate and a tendency toward increased skin temperature. Besides increasing skin temperature, the CDE tended to increase heart rate, especially during the start of the session. Performance data will be discussed in a later report.</p>				
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## SUMMARY

The Air Force Human Resources Laboratory's A-10 flight simulator was used to determine whether the chemical warfare pretreatment drug pyridostigmine bromide (PB) degrades pilot performance and/or physiology. The Advanced Visual Technology System (AVTS) used in the study generated a full-color visual presentation with texturing. A double-blind procedure was followed for administering PB (30 mg, 3 times per day), and a placebo (30 mg, 3 times per day) in a split-plot experiment of crossover design, with 24 A-10 pilots. The pilots were trained over three 55-minute sessions on the following tasks: Task 1, takeoff, patterns, emergency procedure, and landing; Task 2, air-to-air refueling; Task 3, conventional low-angle strafing; and Task 4, low-level ingress/RED FLAG. In two 55-minute test sessions which followed (48 hours apart), all pilots were tested in the simulator. In a double-blind procedure of drug administration, the pilots received PB before one session and a placebo before the other session. During both sessions, 12 pilots wore the chemical defense ensemble (CDE) and the other 12 pilots wore standard flight gear (SFG). Throughout both test sessions (Sessions #4 and #5), data were collected on pilot performance and physiology. Also, other biobehavioral data were recorded prior to, and following, the two test sessions. This report addresses the data collected through physiological recordings and from the pretest and posttest biobehavioral assessments. The principal findings were that the PB dosages led to reports of 27 medical symptoms among 12 (50%) of the pilots. Significantly fewer symptoms (6) were reported by 5 pilots (20%) after they had taken the placebo. Further, on the basis of a spectrum of physiological functions recorded in the study, it appeared that PB had a significant effect upon pilot physiology. Specifically, there was a predictable and significant suppressive effect of PB on heart rate. Also, skin temperature was significantly more elevated in pilots wearing CDE than in those wearing SFG. In support of the findings of the USAF Surgeon General, PB dosages (30 mg, 3 times per day), when given to pilots screened for PB tolerance, is a safe pretreatment drug for Air Force personnel who may be required to operate under chemical warfare threat. Performance data will be discussed in a later report.

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## PREFACE

The present effort was undertaken in support of the USAF Surgeon General at the request of the Joint Working Group on Drug Dependent Degradation of Military Performance (JWGD<sup>3</sup> MILPERF). Funding for the effort was provided by the Walter Reed Army Institute of Research in Washington, DC. The decision was made to conduct the effort at the Operations Training Division of the Air Force Human Resources Laboratory (AFHRL/OT) because the facility housed an A-10 flight simulator with an Advanced Visual Technology System (AVTS) which was available for use in the research.

The authors express appreciation to Mr. Steve Stephens (AFHRL/OTA), Mr. Burl Griffin (AFHRL/OTA), Mr. Tom Dickens (LINK), Ms. Eileen Evans (AFHRL/OT), and Ms. Marge Keslin (UDRI) for their assistance in this effort. Mr. Stephens' thorough understanding of the AVTS, together with his competence in data base development, greatly expedited the conduct of the study. In addition, Mr. Stephens served as program test pilot and performed preflight testing prior to all sessions in which the pilots were tested in the flight simulator. Mr. Burl Griffin was program engineer, and was responsible for numerous technical details that were essential to the study. Mr. Tom Dickens contributed extensively in maintaining the simulator components in good working order. Further, Ms. Eileen Evans provided invaluable assistance in typing drafts of this report and in preparing the written materials preliminary to implementing this investigation. Ms. Marge Keslin presided over the final editing of the report.

The authors also wish to express their appreciation to the pilots from the 343d and 354th Tactical Fighter Wings who volunteered to participate in this research. A special word of thanks is extended to LtCol Larry McNerney (343TFW) and Ms. Marie Bellamy (354 TFW) for their roles in scheduling the study participants. In addition to their regular duties, they arranged for the time to accomplish all of the behind-the-scene coordination necessary to guarantee the success of the study.

We gratefully acknowledge the support of the following personnel from the USAF Hospital, Williams Air Force Base, Arizona, in the medical screening and medical supervision of the study. Col (Dr.) John C. Buckingham, Hospital Commander, authorized the use of medical facilities and consistently backed the participation of those hospital personnel who were critical to the success of the study. Col (Dr.) Lloyd G. Pickering, Flight Surgeon, contributed expert skills in the medical assessment of the volunteer pilots at the time informed consent was obtained for their participation in the study. Further, he made an invaluable contribution to the study through his close medical monitoring of the pilots throughout their stay at Williams AFB. Capt Melissa A. Burkett, Surgical Ward, generously provided facilities in the Ward for use by the subjects and the personnel of the study during the medical screening.

Other essential assistance was provided by 1Lt Dianne C. Davis and MSgt Oscar L. Ellis, Pathology Laboratory (USAF Hospital, Williams AFB, Arizona), and by Dr. Faust Parker, Rothe Development, Inc. (San Antonio, Texas). Lt Davis and MSgt Ellis supervised both the blood draws during an initial medical screening and determination of the changes in acetylcholinesterase levels after intake of pyridostigmine bromide (PB) in this screening. Dr. Faust Parker, Rothe Development, Inc., supervised analyses of the same blood draws for PB activity.

Roche Laboratories (Division of Hoffmann-LaRoche, Inc., Nutley, New Jersey) kindly provided the 30 mg PB tablets (Mestlinon) and the phenotypically identical placebo tablets that were used in the study.

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## EFFECTS OF PYRIDOSTIGMINE BROMIDE ON A-10 PILOTS DURING EXECUTION OF A SIMULATED MISSION: PHYSIOLOGY

### I. INTRODUCTION

The use of chemical weapons in warfare began at an early date in human history. There is evidence that various ancient societies--used chemicals much as do certain contemporary tribes--to poison darts and arrows. In an advance that anticipated the use of gas clouds in World War I, Rome of the second century B.C. resorted to poisonous smoke (Driskell & McTaggart, 1985). It was during World War I that the combatants, first the Germans and then the Allies, shifted from use of a tear gas released in the atmosphere to introduction variously of chlorine, phosgene, and mustard gas. These attacks had their greatest destructive effect on the Russian armies. In the main, though, chemical attacks proved insufficient to overcome the defenses organized against them (Haber, 1986).

After World War I, military commitment was made in Russia, and later elsewhere, to acquire more effective weapons for chemical warfare (CW), as well as more effective defenses against these weapons. Among other means for delivery of chemical weapons, the Soviet developments include rockets, bombs, artillery, ballistic missiles, aircraft, and specialized vehicles. With such devices, the Soviets currently can deliver toxic chemicals as vapors, persistent liquids, solids, powders, or gels (Four Echelon Medical Care System Analysis, 1984). In their various forms, chemical weapons attack the body through several avenues. Entry may be achieved by overt attack and by covert contamination (as by poisoning water or food sources). The chief bodily portals of entry are the skin, the respiratory pathway, the eyes, and the gastrointestinal tract.

Capacity for use of these weapons is integrated into Soviet forces at all levels. In reviewing this Soviet capability, a United States Presidential Commission determined that the Soviet chemical weapons stockpile is several times larger than the usable portion of the United States chemical weapons inventory (Budiansky, 1986). Another estimate put the Soviets at an 8:1 advantage over the U.S. in stockpiled chemical munitions, and at 14:1 in production facilities (Fraile, 1984).

Chemical weapons in the modern Soviet arsenal belong to three main groups as follows: (a) choking agents that affect the respiratory system, (b) blood/blister agents that produce general destruction of body tissue, and (c) nerve agents that interrupt normal functions of the nervous system (Driskell & McTaggart, 1985). Organophosphorus compounds in the third group comprise the most important agents in the Soviet CW arsenal. Small amounts of these compounds in the body can incapacitate or kill because they are unusually efficient in producing lasting ("irreversible") inhibition of the enzyme acetylcholinesterase (AChE). The result is that the neurotransmitter acetylcholine floods across cholinergic synapses and produces paralysis in the muscle cells controlling cardiac and respiratory activity, among other severe effects. Soman (GD), the most potent of the organophosphorus compounds, apparently has become the standard Soviet CW weapon (Four Echelon Medical Care System Analysis, 1984).

The formidable Soviet CW capacity has carried over into actual deployment of chemical weapons in the post-World War II period. Soviet CW agents have been used in offensive operations, as in Afghanistan. Also, Soviet client forces have used CW weapons, as in Laos and Cambodia. Moreover, the CW threat is no longer confined to the Union of Soviet Socialist Republics (USSR) and to Soviet clients. One count has shown that by 1985, 11 nations outside both the North Atlantic Treaty Organization countries and the Warsaw Pact countries possessed chemical weapons (Driskell & McTaggart, 1985). With the spread of CW weapons, there is increased risk that an aggressor chemical attack on the United States could forestall United States Air Force (USAF) retaliation if essential personnel were immobilized (as in shelters), disabled, or killed. Furthermore, the CW threat itself may immobilize personnel. American

Expeditionary Force commanders in World War I reported that military operations were disrupted if personnel presumed that a CW attack was impending (Harris & Paxman, 1982).

The dangers posed by potential enemy CW threats or deployments are understood in the United States. One line of United States response has been the Chemical, Biological, and Radiation (CBR) defense program, a tri-Service effort within the Department of Defense (DOD) that has focused on CW defense capabilities. Early efforts concentrated on developing protective ensembles, detection devices, and shelters. Later efforts were expanded to include distribution of treatment drugs, such as atropine and 2-PAM chloride, to be administered coordinately with an anticonvulsant and muscle relaxant, such as Valium, after exposure to a toxic nerve agent. More recently, study of candidate pretreatment (pre-exposure) chemicals was undertaken because the method of choice for protecting personnel against CW agents may be achieved by combining a "pre-exposure antidote" (pretreatment drug) with "nerve agent antidotes" (treatment compounds) (Whinnery, 1985). The function of a pretreatment drug is to reversibly bind enzyme AChE before exposure to a nerve agent takes place. Reversible binding sets up a transient bond with AChE, and a temporarily protected pool of AChE thereby becomes available to counteract the effects of CW agents (Brimblecombe, 1974). Only a small quantity of AChE, as gradually released from bonding with a pretreatment drug, is required to protect the life of an exposed person.

The search for a safe and effective pretreatment drug in CW has focused on pyridostigmine bromide (PB) Mestinon, made by Roche Laboratories. PB, like other anti-AChE agents, inhibits the destruction of acetylcholine (ACh) by enzyme AChE. PB is the preferred treatment drug for the neuromuscular disorder myasthenia gravis (MG) because PB has a greater duration of action combined with fewer side effects than do other agents to which it is chemically related. Normal persons do not tolerate PB as well as do MG patients; but PB dosages, given at the rate of 30 mg, three times within a 24-hour period, are probably safe (Williams, 1984). Data are lacking concerning the effects of higher PB dosages on physiological functions and on task performance among normal individuals (Williams, 1984). The side effects from PB overdose are, for the most part, classifiable as muscarinic and nicotinic (Koelle, 1985). Symptoms of the former type include nausea, vomiting, diarrhea, abdominal cramps, pupillary contraction, sweating, and increase in peristalsis, in salivation, and in bronchial secretions. Nicotinic symptoms consist mainly of changes in the musculature involving cramps, twitches in muscle groups, and weakness.

In 1983, the United States Army Medical Research and Development Command commenced human studies of PB which addressed questions such as individual differences in tolerance; optimal dosages and dosage frequencies; and duration of drug action (Wannarka, 1984). This effort was expanded in the United States Army-directed tri-Service program, the Joint Working Group Drug Dependent Degradation of Military Performance (JWGD<sup>3</sup> MILPERF). From the various lines of research that have been undertaken with regard to the usefulness of this drug, the Office of the Air Force Surgeon General concluded that PB is the pretreatment drug of choice for defense against lethal nerve agents (DeHart, 1987). Apparently, the antidotes pralidoxime (2-PAM chloride) and atropine are inadequate in treatment of personnel who have been exposed to nerve agents, particularly Soman (GD), unless these personnel have been pretreated with PB (DeHart, 1987).

Nonetheless, there may be contraindications to the use of PB in the context of certain Air Force operations. From what little data there are, there is indication that PB doses can degrade performance of complex tasks while leaving simpler tasks unaffected (Driskell & McTaggart, 1985). These findings carry an implication that PB, which does not easily cross the blood-brain barrier (Bernstein, 1983; Koelle, 1985), may nonetheless affect the central nervous system. Such effects are possible because PB may change the balance of brain bioamines at dosages too low to produce detectable somatic signs (Bignami, Rosic, Michalek, Milosevic, & Gatti, 1975; Calabrese, 1983). Confirmation that PB degrades behavior would have implications for use of the drug to protect personnel assigned to demanding, complex duties such as those required of aircrews



engaged in military operations. In the present study, the possibility that PB can degrade psychophysiological performance was explored by assessing how efficiently mission-ready pilots pretreated with PB (or a placebo) and wearing standard gear or protective clothing carried out a simulated flight. During execution of the simulated mission, the pilots wore either standard flight gear (SFG) or the chemical defense ensemble (CDE) so that PB effects on functioning in a simulated chemical warfare environment could be better identified.

## II. METHOD

### Design

The experiment reported in this investigation was a double-blind study of split-plot design in which there were counterbalanced presentations of the within-group treatment. Three training sessions (Sessions #1, #2, #3) preceded, by 48 hours, the two test sessions (Sessions #4 and #5) in which the study data were collected. The summary representation presented in Table 1 shows the between-groups factor was apparel (chemical defense ensemble [CDE] versus standard flight gear [SFG]). One within-groups factor was dosages (PB versus placebo tablets). The other within-groups factor of special interest in the analyses of the physiological data was that of temporal effects (times) which addressed functioning during the successive task elements of each 55-minute test session.

Table 1. Split-Plot Design of Study

CDE worn			SFG worn		
PB administered			PB administered		
Subject	Session #4	Session #5	Subject	Session #4	Session #5
A	Yes	No	K	Yes	No
B	No	Yes	L	No	Yes
C	No	Yes	M	No	Yes
D	No	Yes	N	No	Yes
E	Yes	No	O	Yes	No
F	Yes	No	P	Yes	No
G	No	Yes	Q	No	Yes
H	Yes	No	R	Yes	No
I	Yes	No	S	Yes	No
J	No	Yes	T	No	Yes

### Human Use Committee

The research protocol for the study was found to be in conformity with AFR 169-3 (15 Jul 85), Use of Human Subjects in Research, Development, Test, and Evaluation, by the Air Force Human Use Committee, Bolling Air Force Base, on 17 December 1986, and was approved by the Air Force Surgeon General, Bolling AFB, on 18 December 1986. Also, the protocol was found in compliance with all DoD components of DoD Directive 3216.0, Protection of Human Subjects in DoD-Supported Research, by the Human Use Review Office, U.S. Army Medical Research and Development Command, Fort Detrick, Maryland, on 18 February 1987. A Notice of Claimed Investigational Exemption for a New Drug for permission to use PB in tests on human volunteers was submitted to the Food and Drug Administration (FDA), Department of Health and Human Services, on 20 July 1986. On 21 August 1986, the FDA approved PB as an Investigational New Drug (IND #24,480) for use with human volunteers in the study.

## Subjects

The volunteers for the study were 24 mission-ready A-10 pilots who were stationed at Eielson Air Force Base, Alaska (12 pilots); England Air Force Base, Louisiana (2 pilots); and Myrtle Beach Air Force Base, South Carolina (10 pilots). Prior to the study, all of the volunteers were screened at their home bases for tolerance to PB in conjunction with an Air Force-wide program. Also, before the pilots arrived at AFHRL, Williams Air Force Base, Arizona, to participate in the study, they were randomly assigned either to a group that wore the chemical defense ensemble (CDE) or to a group that wore standard flight gear (SFG) during Sessions #4 and #5. Pilots assigned to wear CDE during testing wore their own helmets and chemical defense face masks. The mean age of the pilots in the CDE group was 29.0 years, with a standard deviation (SD) of 3.1 years; their mean body weight was 77.9 kilograms, with an SD of 9.4 kg. Matching values for the SFG group were 29.5 years (SD = 4.6 years) and 87.1 kg (SD = 9.2 kg).

At the time the pilots volunteered for the study, they were informed that the primary benefits of the study were for the defense posture of the United States and that the Air Force commitment to conduct the study was made with this intention. The pilots were also informed, however, that there were individual benefits for the participants. Among these benefits was the opportunity to practice a variety of flight-related activities in a "state-of-the-art" A-10 flight simulator. Another benefit for 50% of the participants was the opportunity for experience in flying a simulated mission while wearing CDE.

## Apparatus

### Simulator

The flight simulator used in the study was the AFHRL A-10 flight simulator. A list of operational cockpit instruments, and graphic displays of the layout of the cockpit, may be found in Appendix A. The simulator does not have a motion system. The G-seat and G-suit were not used in this study.

### Visual

The Advanced Visual Technology System (AVTS) is 10-channel Computer Image Generator (CIG) capable of generating, every 33.3 milliseconds (ms), 6,000 edges, 4,000 point features, 1,000 circular features, and 7 moving models. All 10 channels support texturing, a feature which provides motion and attitude cues considered essential for low-level flight and other air-to-surface missions. Ferguson, Cody, and Petrie (1986) have documented system specifications for the AVTS. The AVTS full-color visual imagery was displayed in a dodecahedron equipped with color light valves.

### Data Base

Based on real-world data from the Defense Mapping Agency (DMA), an area of 10,000 square nautical miles (nm<sup>2</sup>) was modeled. Included was Nellis Air Force Base, Nevada, and the nearby RED FLAG ranges. Most of the data base contains terrain elevation and cultural feature data. This AVTS data base represents, as accurately as possible within the constraints of the system, the actual geographic areas. Detailed specifications of this data base may be found in Ferguson et al. (1986).

### Performance Measures

The basic element in the performance measurement system was a VAX system (Digital Equipment Corporation) for storage of the behavioral data. Software needed for acquisition of the data recorded on the VAX was developed by AFHRL contractor personnel. Also, the VAX supported a variety of statistical software packages that were used for analyses of the data.

### Biobehavioral Measures

A Honeywell Simultrace VR-12/bN recording system was used to record the following: electrocardiogram (ECG), 1 channel; electromyogram (EMG), 2 channels; respiration, 1 channel; and skin temperature, 2 channels. Leads from the Simultrace recorder were connected to an isolated patient junction box (Model IPJB/6) that was mounted immediately behind the A-10 cockpit. Electrodes and thermistors that were attached to the different subjects fed into the junction box. Three-lead patient cables (10 feet) were used to record ECG and EMG activity. Respiration was monitored through a branched cable and a five-wire respiration lead set. Thermistors (Yellow Springs Instrument Co.) were used to record skin temperatures. Records of heart rates in beats per minute (bpm) and respiratory rates in respirations per minute (rpm) were taken at 1-minute intervals throughout each of the two test sessions (Sessions #4 and #5). All other physiological records obtained in the study were read from strip charts.

Physiological data were recorded on the Honeywell at 400 Hertz (Hz). Pilot performance data were recorded at 10 Hz. Preprogramming and operator input at the Instructor/Operator Station (IOS) determined content/start/stop of the data collection. A High Speed Data (HSD) communication link connected the IOS with the programmable interface and collection systems (PICS). Both the physiological and performance data were synchronized on the PICS and then were stored on the VAX.

### Other Measures

A hand dynamometer (Lafayette Instrument Co.), with a range from 0 to 100 kg, was used to test grip strength in each hand. Also, two questionnaires were administered to assess subjective reactions, and a third instrument was used to identify individual food and fluid intakes. The first questionnaire was a checklist that allowed the pilot to identify which, if any, of 54 listed symptoms he experienced after taking two separate series of three tablets (PB and a placebo). Severity of reported symptoms was rated on a 7-point scale (1 = slight; 7 = severe). The second device was the Crew Status Survey (School of Aviation Medicine, Brooks Air Force Base, Texas; Form 202, April 1981), which probed "subjective fatigue" and "workload estimates" among the pilots at the end of test sessions in the flight simulator. Again, ratings were made along 7-point scales in which (1) represented the lowest and (7) the highest values. The third questionnaire was used to determine whether the pilots had refrained, as asked, from caffeinated beverages and from use of tobacco over the 24-hour period preceding sessions in which the pilots were tested in the flight simulator. Copies of the symptom checklist and Caffeine/Tobacco Questionnaire may be found in Appendix B.

### Medical Equipment

A medical aid station adjacent to the A-10 flight simulator was equipped with a stowable cot, a supply of supplementary oxygen, a Sparkit augmented with atropine, Di-Gel, blood pressure cuffs, and an Ambubag.

## Tasks

The scenario used throughout the study was a "mission" of 55 minutes in duration, divided among four segments as follows: (a) takeoff and "pattern" work with an embedded emergency procedure (15 minutes), (b) inflight air-to-air refueling (AAR) from a simulated tanker (8 minutes), (c) conventional low-angle strafing (12 minutes), and (d) low-level ingress/"RED FLAG" (20 minutes). All of the events took place in a visual environment over realistically modeled land masses and specific terrain areas of the Nellis/RED FLAG Range areas of Nevada. Realistic types and concentrations of aircraft, targets, and threats were programmed in the different segments, which proceeded as follows.

### Takeoff/Patterns/Engine-Out/Landing

The pilot took off from Nellis AFB, climbed to 4,000 feet mean sea level (MSL), and leveled off. He completed the pattern with feedback from the IOS and did a "touch and go." On his second pattern, he "lost" an engine and had to take appropriate action to land the plane. Time allotted for this task was 15 minutes. The simulator froze at the end of 15 minutes, and the visual display was cleared of all CIG imagery.

### Air-to-Air Refueling

In this task, the pilot rendezvoused with a KC-135 tanker and attempted to refuel. The simulator was reinitialized with both engines working properly for the duration of this task. At the point of initialization, the pilot was 1,000 feet behind a KC-135 moving at 200 knots with a working boom. The pilot tried to adjust his flight parameters to match those of the tanker and to hook up and to take on as much fuel as possible. At 8 minutes, regardless of refueling success, the visual display was cleared, and the simulator was put on freeze.

### Conventional Low-Angle Strafing

For the third task, the pilot strafed a target on a conventional gunnery range from a visual low-angle pattern. The Nellis conventional range layout was modeled for this task. The pilot strafed the target as many times as possible during the 12-minute session. Pilots received feedback on percentage of hits.

### Low-Level Ingress/RED FLAG

The pilot was initialized for low-level penetration into a tactical target area. In the initial part of the segment, the pilot navigated a preplanned route of 30 nautical miles to the target area at an altitude of 50 to 500 feet above ground level (AGL). At the initial point (IP), the pilot proceeded into the target/threat area with the intention of destroying the command post. From this point, the pilot was subjected to threats from anti-aircraft artillery (AAA) and surface-to-air missiles (SAMs) as a realistic function of his attack tactics. After attacking the command post, the pilot could make additional passes or go on to attack three other target areas. The pilot continued to be susceptible to threats. When he hit a target, a smoke plume appeared in the visual scene over the target to indicate a kill. The AAA and SAMs could also be killed. When the pilot was killed, the visual scene turned red for a fraction of a second. If the pilot hit the ground, he did not "die." If a simulator malfunction occurred in the target area, the pilot was restarted at the IP. If a malfunction occurred during low-level ingress, the pilot was initialized

at the nearest checkpoint. After 20 minutes, the session terminated. Complete details on these tasks may be found in Appendix C.

## Measurements

### Performance

The performance measures recorded by the study software included both common measures and segment-specific measures. The measures recorded that were common to all four segments were as follows: aircraft position, acceleration, velocity, pitch, roll, and control inputs. The segment-specific measures included the following: Refueling: time connected with boom and number of disconnects; Strafing: airspeed, G-loadings, range at open fire, range at cease fire, number of rounds fired, number of hits, and number of crashes; "RED FLAG"-Penetration: airspeed, G-loadings, and number of crashes; "RED FLAG"-Tactics: airspeed, G-loadings, number of kills, number of times killed, number of rounds fired, range at open fire/cease fire, number of engagements, and number of times threats in range detected. A complete list of all measures recorded for each task may be found in Appendix D.

### Psychomotor and Physiological

The physiological recorder system used in the present application was evaluated in pretests and was proven free from hardware problems. No electrical noise from the flight simulator or other sources in the facility contaminated the physiological records.

One psychomotor activity (handgrip strength) and several physiological functions were recorded. Bilateral handgrip strength was assessed in the study because Graham and Cook (1984) found this task ranked, along with several other psychomotor tasks, as a most useful gauge of PB effects among a variety of tests in a battery that covered psychomotor, sensory, perceptual, and cognitive functions. Further assessment of muscle strength presumably provided (Graham & Cook, 1984) a quick determination in individual cases of how far recovery from the PB dosages had proceeded before testing was started in the flight simulator.

The physiological variables were monitored throughout all sessions at the same settings on the Honeywell recorder and at a chart speed of 25 centimeters per second (cm/sec). Adhesive electrodes (Honeywell) attached to the skin were used to monitor elements in the following areas of physiological activity: baseline muscle contractions (EMG), cardiac activity (ECG), and respiratory functions. Skin temperature, however, was monitored by means of thermistors. Before the pilots were tested in Sessions #4 and #5, the skin underlying the probes was scrubbed and cleaned with Omniprep (D.O. Weaver & Co.) to remove dead layers of cells, as well as oil and salt. Also, care was taken to isolate contact areas beneath the electrodes so that the cleansing fluid did not produce a leakage path between electrodes. After each use, the electrodes were removed and discarded.

*Handgrip Strength.* Handgrip strength was assessed by use of the Lafayette dynamometer. Each assessment consisted of four trials in which the two hands were tested alternately. At the start of each trial, the tested arm was held cocked at the elbow and parallel to the floor, and the face of the dynamometer was turned away from the pilot. A trial ended when the pilot indicated, verbally or otherwise, that grip strength had been maximally exerted.

*Cardiac Activity.* Several measures of cardiac activity were recorded. These measures included the following: heart rate in beats per minute (bpm) and two measures of the QRS

complex. The QRS complex consists of a downward stroke in electrical activity (Q wave), an upward deflection (R wave), and a following downstroke (S wave). One QRS complex measure treated the temporal length (duration) of QRS complexes. The second QRS complex measure focused on the amplitude of the R wave to determine the systolic force of the heartbeat. The recordings of cardiac functions were obtained through use of precordial leads. The positive lead was attached to the center of the chest just below the collar bone, and the negative lead was placed on a line with the left armpit at the level of the fifth rib. The indifferent lead was placed just to the left of the spine in an area of low muscle activity (the thoracolumbar fascia).

*Respiration.* Respiratory rate (cycles/minute) and volume were analyzed. Both variables were recorded by an array of four electrodes that were attached laterally in the fifth intercostal region.

*Neuromuscular Activity.* Because neuromuscular activity was recorded during movement, amplifier gain in the Honeywell recorder was reduced from the high gain that is needed for measurements involving passive subjects. Muscle potentials in the range of 1 to 25 per second were recorded by electrodes that were attached to the skin overlying each superficial latissimus dorsi muscle (mid-dorsal trunk area). The electrodes were placed 3.0 cm apart along the cephalocaudal line above each muscle.

*Skin Temperature.* Skin temperature was monitored by two thermistors. A latex sweat band (6.5 millimeters [mm] thick) held the thermistors against the skin overlying the left and the right trapezius muscle at the junction of the dorsal neck and shoulders.

### Procedure

Prospective volunteer subjects for the study were mailed three items that described the aims of the study and covered duties of the participants during the different 5-day periods of data collection. The items were as follows: (a) an invitation that explained the aims of the study, (b) an informed consent form that further explained the study goals and described how PB affects the nervous system and what might be the side-effect of the drug, and (c) a day-to-day schedule of each participant's activities in the investigation.

After their arrival at Williams AFB, the pilots participated without deviation in all iterations of the experimental procedure over successive 5-day test periods.

#### Sunday

One of the researchers associated with the study met each group of three pilots at the time the volunteers checked in at Williams AFB. The researcher answered questions concerning the mailings and familiarized the pilots, as needed, with the location of base facilities. The pilots were instructed to fast (except for water) for the 8-hour period preceding their appearance at the Williams AFB USAF Hospital at 0600 on the following day.

#### Monday

Upon arrival at the hospital, the pilots were screened for tolerance for PB. A flight surgeon assigned to the study discussed the risk factors for participants in the study and supervised signing the informed consent statements. Then, whole blood (7.5 milliliters [ml]) was obtained

from each pilot, who next took one (oral) 30 mg PB tablet (Mestinon, Hoffmann-LaRoche, Inc.). During the next 2 hours, the group heard a videotaped lecture on the flight scenario and had questions concerning the study answered by personnel assigned to the study. Two hours after the PB tablets had been taken, the pilots underwent a second 7.5 ml blood draw.

At 0930 hours, 1030 hours, and 1130 hours, the three A-10 pilots in the group of volunteers, individually and successively, undertook a "familiarization" session (Session #1) in the A-10 flight simulator. Each flight was carefully supervised by one of the researchers in the Instructor/Operator Station (IOS), who used a two-way communication system in closely monitoring and guiding the performance of each pilot. The procedure was repeated with the different pilots at 1330 hours, 1430 hours, and 1530 hours. In Session #2, however, the amount of feedback given to the pilots on their performance, though tailored to the individual, was significantly reduced.

### Tuesday

Session #3, the last of the training sessions, was conducted with the pilots at 0800 hours, 0900 hours, and 1000 hours, respectively. The experimenter held feedback on performance to the minimum while the three pilots individually repeated the run through the scenario.

Thereafter, a USAF flight surgeon supervised the first of two series of double-blind administrations of PB and placebo tablets (30 mg, 3x/day) with the pilots. If PB tablets were taken in the first series, then in the double-blind procedure placebo tablets were taken in the second series. Administrations of the tablets began with the different pilots at 1500 hours, 1630 hours, and 1800 hours, respectively, and continued until each pilot had taken three tablets at 8-hour intervals.

### Wednesday

The pilots reported to the Operations Training Division of the Air Force Human Resources Laboratory (AFHRL/OT) 30 minutes before the start of Session #4. At that time, the pilots were tested for handgrip strength, were questioned in detail concerning their food and fluid intakes over the preceding day, and were asked to complete the checklist which covered the spectrum of symptoms that may be associated with PB intake. The pilots either wore SFG (50% of the pilots) or wore CDE (the other 50%) in Session #4, which began for the different pilots at 0830 hours, 1000 hours, and 1130 hours. In this arrangement, each pilot began the session 1.5 hours after the third tablet in the first series of administrations had been ingested. At the end of the session, each pilot completed the Crew Status Survey as to his subjective estimates of both the fatigue induced by the task and the imposed workload.

### Thursday

None of the pilots were tested on this day. The interruption in the study provided time for drug clearance from the body to occur among the pilots who had been given PB in the first series of three tablets. The USAF Flight Surgeon, however, supervised the second series of double-blind administrations of tablets (30 mg, 3x/day) to the three pilots. The pilots followed the same schedule in taking the tablets that had been used with the first series of tablets.

### Friday

The procedure followed in conducting Session #5 repeated that followed with Session #4. Thus, the pilots were tested while wearing the same apparel in both sessions of data collection. Bilateral handgrip was again tested, and the pilots completed the checklists and the survey of

dietary behavior. The code to the double-blind procedures was broken after the last of the three pilots who were tested in a given week had completed Session #5. The three pilots and the experimenters then learned the order in which the pilots had received the three PB tablets and the three placebo tablets. At this point, upon the approval of the Flight Surgeon, the pilots were released.

### III. PHARMACOLOGICAL AND BIOPHYSICAL RESULTS

#### Pharmacological Findings

##### Screening Test

A single 30 mg dose of PB markedly inhibits blood ChE after 30 minutes (Driskell & McTaggart, 1984). This inhibition of blood ChE reaches a peak level 1.7 hours after oral intake if the person has been fasting, or in about 3.2 hours in a nonfasting person (Aquilonius, Eckernas, Hartvig, Lindstrom, & Osterman, 1980). The 7.5 ml blood draw, which was taken immediately prior to testing each pilot for PB tolerance, served to provide baseline readings for plasma ChE as follows:  $\bar{M} = 4,703$  (SD 1,055) units/liter (U/L) of plasma (range, 2,132 - 6,447 U/L). Baseline plasma PB readings were zero. Changes in the blood that resulted from (oral) PB administrations to the 24 fasting pilots in this study are shown in Table 2. The results in Table 2 describe PB effects 2.0 hours after one 30 mg PB tablet had been taken by each pilot in the screening test. At that time, apparently, PB was significantly present in the plasma of all 24 pilots, and inhibitory effects of the drug on ChE were observable in the majority. There were apparently marked individual differences in both categories of plasma responses to PB. In none of the pilots, though, did ChE inhibition reach the point of 40% ChE inhibition at which the drug may begin to have medically significant effects. There was, however, little concordance between degree of plasma PB and ChE changes among the different pilots. The correlation (Pearson product moment correlation) between the two variables was nonsignificant ( $r = +.38$ ,  $p > .05$ ).

Table 2. Plasma PB and ChE Inhibition

Plasma PB (ng/ml) <sup>a</sup>		ChE inhibition (%) <sup>b</sup>	
$\bar{M}$	9.9	$\bar{M}$	11.0
SD	4.8	SD	7.3
Range	3 - 21	Range	0 - 26

Note: Blood draws used for the analyses occurred two hours after single oral doses of 30 mg PB tablets.

<sup>a</sup>Roth Development, Inc., San Antonio, TX.

<sup>b</sup>Pathology Laboratory, USAF Hospital, Williams AFB, AZ.

##### Symptom Picture

When the pilots reported individually for testing on Sessions #4 and #5 (Wednesdays and Fridays), they were asked on each occasion to guess whether the drug or the placebo had been taken during the double-blind administration of tablets (30 mg, 3x/8 hours) that preceded both sessions. This inquiry took place 90 minutes after the last tablet in each series of three tablets had been taken. Also, the pilots were asked to state what, if any, symptoms they experienced that they could attribute to the tablets taken in a particular series. For that purpose, the pilots completed a checklist describing 54 types of symptoms that are potentially associated with PB overdosage. Nonlisted categories could be added at the discretion of the pilot.



### Symptom Rates

Among the 24 pilots, 12 of them reported experiencing symptoms after taking PB (30 mg, 3x/day) in the double-blind procedure of the experiment. In contrast, five pilots experienced symptoms after the placebo (30 mg, 3x/day) in the same double-blind procedure. The different symptom rates, shown in Table 3, for the two sets of reports were contrasted by the test for the difference between two correlated proportions (Bruning & Kintz, 1987). The difference was significant ( $z = 2.15$ ,  $p < .05$ ).

Table 3. Symptomatology

Number of symptoms	N (%) of pilots reporting symptoms	
	After taking PB	After taking Placebo
1	4 (16.7%)	4 (16.7%)
2	5 (20.8%)	1 (4.2%)
3	1 (4.2%)	0
4	1 (4.2%)	0
4+	1 (4.2%)	0
TOTALS	12 (50.0%)	5 (20.8%)

### Type and Severity of Symptoms

Every symptom that was described by the pilots was named in the checklist of 54 symptoms. Pilots who actually received PB attributed to the tablets a total of 28 symptoms, belonging to 17 different symptom types. Among the symptoms commonly associated with PB, those most frequently reported by the pilots (by type and frequency) were as follows: stomach gas and/or burping (6), fatigue and/or muscle fatigue (6), and confusion and/or giddiness (5). Other symptoms included headache (2), increased salivation (1), dry mouth (1), rapid heartbeat (1), sweating (1), tingling (1), itching (1), irritability (1), blurred vision (1), and increased bowel activity (1). The six symptoms experienced by the five pilots who were taking the placebo were as follows: drowsiness (2), stomach gas (2), fatigue (1), and headache (1).

When listing the kinds of symptoms, if any, that attended taking one or the other series of tablets, the pilots marked the severity of the symptom(s) on a 7-point scale (1 = "slight"; 7 = "severe"). Mean ranking for symptoms associated with taking PB was 1.3 (SD 0.6, range 1-3). For symptoms associated with taking the placebo, the mean ranking was 1.5 (SD 0.8, range 1-3). Thus, symptom severity associated with taking PB was about as great as that resulting from taking a placebo.

### Identifying Dosages Received

Data summarized in Table 4 show that 14 of the 24 pilots (58.3%) guessed correctly which were the PB tablets and which were the placebos in the two series of three-tablet administrations. Of the 10 guessing incorrectly, 3 pilots (12.5%) guessed incorrectly both times; the other 7 pilots, even though they had been told that they would receive PB one day and placebo another, guessed that the PB was given in the two series (3 pilots) or that the placebo was given in both series (4 pilots).

**Table 4. Identifying Dosages Received**

Correct guesses in:	N of pilots guessing correctly	Plasma PB (ng/ml)		
		M	SD	Range
Both series	14	10.0	4.9	3.0 - 21.0
One series <sup>a</sup>	7	10.3	5.9	4.0 - 21.0
Neither series	3	8.3	1.5	7.0 - 10.0
Plasma ChE inactivation (%)				
Both series	14	9.3	6.3	1.5 - 23.5
One series <sup>a</sup>	7	14.4	5.9	8.2 - 22.2
Neither series	3	11.2	11.0	0.5 - 26.4

<sup>a</sup>Pilots stated (incorrectly) that the same compound was given in the two series.

### Biophysical Measurements

#### Handgrip Strength

All pilots were tested for handgrip strength in the left hand (L) and the right hand (R) just prior to Sessions #4 and #5 in the flight simulator. The tests were aimed at assessing whether a series of PB dosages (30 mg, 3x/8 hours) affected muscular strength through its effects on cholinergic activity at neuromuscular junctions. Possible effects of social facilitation on performance were reduced by asking for a "personal best" response and by having no observer other than one experimenter present during testing. The hand dynamometer (Lafayette) used in the tests was adjusted comfortably to fit the handgrip of each subject. Then, upon instruction, the pilot squeezed the dynamometer handle against its base with one hand until he was satisfied that his strength had been exerted maximally. A reading was taken and shown to the pilot. The dynamometer was then reset for a test with the pilot's other hand. Testing was repeated until two records were obtained for each hand. The pilots were assigned at random to testing in LRLR order in one session and RLRL order in the other test session.

Inspection of Table 5 shows a slight superiority of the right hand over the left hand in grip strength. There was not, however, an indication of a change in grip strength in either hand attributable to PB dosages. Comparisons of the results summarized in Table 5 for each hand were performed by means of the McNemar test for significance of changes (Siegel, 1956). Effects of PB on handgrip strength were nonsignificant ( $p > .30$ ) for both the left hand ( $\chi^2[1, N = 24] = 0.41$ ) and the right hand ( $\chi^2[1, N = 24] = 0.70$ ).

**Table 5. Handgrip Strength**

	LH grip strength (Kg)		RH grip strength (Kg)	
	Placebo	PB	Placebo	PB
M	58.3	56.7	61.0	60.5
SD	10.3	11.0	11.6	11.6
Range	36.0 - 78.2	39.0 - 79.5	42.0 - 84.2	38.0 - 86.8

#### Physiological Recordings

The Honeywell biophysical recording system was used to develop strip chart records during Sessions #4 and #5 in the flight simulator. Ambient temperature in the bay which housed the

simulator was held at 19.5° Celsius (C) and the relative humidity was 55%. Several sets of physiological variables, which included various cardiac, respiratory, and muscle potential functions, as well as body temperature (skin surface), were monitored by the Honeywell system at a chart speed of 25 mm/sec. During the test sessions (Sessions #4 and #5), the different measures were recorded for both the 12 pilots who wore CDE and the 12 pilots who wore SFG. The recordings were made through Honeywell disposable adhesive electrodes. The skin at recording points was thoroughly cleansed with electrode paste, pumice cleanser, and alcohol before the electrodes were placed. The fine wire leads were pigtailed together and passed through the back neck of the CDE or SFG to a junction box situated behind the pilot's seat in the simulator. The leads from the thermistors were heavier and necessitated taping them to the skin and clipping them to the suit after they passed through the neck opening of the suit. In the two test sessions, the pilots were thus monitored on one occasion after they had taken the series of PB dosages (30 mg, 3x/8 hours) and, on the other occasion, after they had taken a series of placebo dosages (30 mg, 3x/8 hours). The biophysical data recorded during the two 55-minute test sessions were analyzed for the following main effects (factors): gear (CDE versus SFG), dosages (PB versus placebo), and times (start versus end of the test sessions).

**Cardiac Activity.** Mean heart rates, in beats per minute (bpm), for the 12 pilots outfitted in CDE and the 12 pilots who wore SFG are presented in Table 6. The data recorded in Table 6 show the effects of PB versus the placebo on mean heart rates for each of the four sets of tasks that were performed during Sessions #4 and #5. Table 6 indicates the occurrence of some suppressive effect of PB on heart rate. This was confirmed by Analysis of Variance (ANOVA). Significant differences were found between the CDE group and the SFG group at the start of the test session for heart rate ( $F_{[1,22]} = 5.22, p = .032$ ). At the end of Task 3 (Target Strafe), a significant Gear by Drug interaction was observed ( $F_{[1,22]} = 5.09, p = .034$ ). Significant effects of PB on heart rate were found for different points of the test sessions. At the outset of Task 1 ( $F_{[1,22]} = 6.72, p = .017$ ) and at the end of Task 3 ( $F_{[1,22]} = 4.33, p = .049$ ), heart rates were significantly lower under the PB condition than under the placebo condition. Nevertheless, for reasons treated in the Discussion section, nonsignificant PB effects on heart rate were found at the end of Task 1 ( $F_{[1,22]} = 0.48, p = .496$ ), at the end of Task 2 ( $F_{[1,22]} = 2.42, p = .134$ ), and at the completion of Task 4 ( $F_{[1,22]} = 1.23, p = .280$ ).

Table 6. Heart Rates

Session elements	Mean heart rates (bpm) during test sessions				
	Standard flight gear (SFG)		Chemical defense ensemble (CDE)		SEM <sup>a</sup>
	PB	Placebo	PB	Placebo	
Start Task 1	73.8	83.4	84.0	94.8	3.9
End Task 1	82.5	89.8	94.1	91.6	3.5
End Task 2	88.8	90.8	83.0	95.4	4.6
End Task 3	82.0	81.5	85.0	97.4	2.9
End Task 4	95.1	93.8	93.6	103.5	3.9

<sup>a</sup>Standard error of the mean.

Analyses were also performed on two other measures of cardiac activity in the pilots. One analysis treated records that were obtained for the QRS complex, which is composed of three cardiac waveforms. This measure was taken because the duration of the QRS complex tends to decrease during effort. The diminished length of time for the QRS complex is attributable to the improvement in ventricular function required to meet increased circulatory demand. Therefore, the presumption was that the A-10 pilots would have shown a significant decrease in durations of the QRS complex if any of the main effects (Gear or Drugs) imposed greater demands on the pilots than was the case under control conditions. The analysis, however, showed that the interactions and main effects were nonsignificant ( $p > .10$ ). A second analysis

concerned the force of the R waves (principal wave in the systolic [squeezing] phase of the heartbeat) throughout the test sessions. The results from analysis of the R wave data also showed no significance ( $p > .10$ ) for either the interactions or main effects.

**Respiration.** Results for respiratory rates (respirations per minute [rpm]) during testing in Sessions #4 and #5 are summarized in Table 7. Inspection of Table 7 suggests that respiratory rate was not affected during the sessions in any obvious manner by the experimental variables of Gear or Drug. This inference was confirmed by the data analysis. A like pattern of non-significant results was obtained in an analysis of respiratory amplitudes. These amplitudes were recorded as changes in position of the chest as were produced by the activity of the respiratory muscles during the inspiration and expiration phases of breathing cycles.

**Table 7. Respiratory Rates**

Mean respiratory rates (breaths/min) during test sessions					
Session elements	Standard flight gear		Chemical defense ensemble		
	(SFG)		(CDE)		
	PB	Placebo	PB	Placebo	SEM <sup>a</sup>
Start Task 1	19.8	21.9	20.6	19.2	1.9
End Task 1	21.3	24.3	21.0	19.8	1.6
End Task 2	21.8	22.1	20.0	19.1	1.3
End Task 3	23.9	21.9	20.6	20.5	2.1
End Task 4	21.1	22.8	23.4	22.8	1.3

<sup>a</sup>Standard error of the mean.

**Heart Rate (bpm)/Respiratory Rate (rpm) Ratios.** Activity of the circulatory and respiratory processes is governed by internally located mechanisms and externally by linked pathways in the autonomic nervous system. Thus, receptors in the lungs that respond to stretch accelerate heart rate through inhibiting cholinergic activity in the vagus nerve connections to the heart. Ratios of heart rate to breathing rate in healthy young adults range from 4:1 to 5:1 during the course of everyday life. Deviations from these ratios in young adults may be produced through a variety of factors which include temperature, plasma electrolyte concentrations, and various hormones. The most important factor, however, in increasing the size of this ratio is muscular effort (Berger, 1982). Presumably, muscular effort was the principal factor effecting changes on the bpm/rpm ratios shown in Table 8. Inspection of Table 8 shows there were differences in the bpm/rpm ratios between the 12 pilots who wore CDE and the 12 pilots who wore SFG, as well as between the drug and the placebo conditions. In both instances, the differences in bpm/rpm ratios were not significant at the .05 level, except for one gear by dosages interaction observed at the end of the session ( $F[1,22] = 4.40$ ,  $p = .048$ ).

**Table 8. Heart Rate (bpm)/Respiratory Rate (rpm) Ratios**

Mean heart rate (bpm) and mean respiratory rate (rpm)					
Ratios during test sessions					
Session elements	Standard flight gear (SFG)		Chemical defense ensemble (CDE)		
	PB	Placebo	PB	Placebo	SEM <sup>a</sup>
Start Task 1	4.02	4.09	4.34	5.26	.38
End Task 1	4.05	3.98	4.68	4.78	.29
End Task 2	4.49	4.37	4.39	5.14	.43
End Task 3	3.66	4.16	4.44	5.18	.31
End Task 4	4.91	4.33	4.13	4.62	.26

<sup>a</sup>Standard error of the mean.

**Neuromuscular Activity.** The size of muscular contractions in the 1 to 25 Hz range, scored as upward pen excursions on the Honeywell strip charts, was recorded by means of electrodes attached to the skin of the middle back overlying the left and right superficial latissimus dorsi muscles. Analyses of the data showed that none of the interactions and none of the main effects were significant.

**Skin Temperature.** Skin temperatures were measured in degrees Celsius ( $^{\circ}\text{C}$ ). The skin areas most readily accessible to temperature recordings in pilots wearing CDE were the skin overlying the left and right trapezius muscles of the lower dorsal (back) neck. Temperature means for the skin above both trapezius muscles are presented in Table 9 for the two test sessions in which PB or the placebo was administered. Inspection of Table 9 indicates that skin temperature became elevated during the test sessions in both the group wearing CDE and the group wearing SFG, but that temperature increase was greater in the CDE group. The measures of temperature increase for gear and for dosages proved significant. Analysis of the recorded data for the factor of gear did not reveal a significant difference between the CDE and the SFG groups at the start of Task 1 ( $F[1,22] = 3.45, p = 0.077$ ). By the end of Task 1, however, the gear main effect showed that skin temperature was significantly higher in the CDE group than in the SFG group ( $F[1,22] = 8.68, p = .007$ ). Significantly higher skin temperatures in the CDE group were found similarly at the end of Task 2 ( $F[1,22] = 14.50, p = .001$ ), Task 3 ( $F[1,22] = 14.49, p = .001$ ), and Task 4 ( $F[1,22] = 15.15, p = .001$ ). Furthermore, the difference between skin temperatures at the start of Task 1 and the end of Task 4 was also significant ( $F[1,22] = 4.81, p = .05$ ). PB was found to increase skin temperature only at the end of Task 3 ( $F[1,22] = 5.46, p = .029$ ).

**Table 9. Skin Temperature ( $^{\circ}\text{C}$ ) Fluctuations**

Session elements	Mean skin temperature ( $^{\circ}\text{C}$ ) during test sessions				
	Standard flight gear (SFG)		Chemical defense ensemble (CDE)		SEM <sup>a</sup>
	PB	Placebo	PB	Placebo	
Start Task 1	30.9	30.9	32.1	31.8	0.3
End Task 1	33.0	32.6	34.3	33.9	0.3
End Task 2	33.5	33.1	35.1	34.6	0.2
End Task 3	33.7	33.3	35.4	34.7	0.2
End Task 4	33.8	33.8	35.5	34.9	0.3

<sup>a</sup>Standard error of the mean.

### Self-Ratings

The Crew Status Survey was used to obtain subjective fatigue and workload estimates from the pilots. At the end of Sessions #4 and #5, all pilots completed 7-point self-rating scales in both of the assessed categories. Results from the sets of self-ratings were treated by ANOVA.

### Subjective Fatigue

Inspection of Table 10 indicates that subjective judgments of post-session fatigue ranged from 1 to 5 within the 7-point scale. Whether or not the pilots had been dosed with PB did not appear to affect these judgments significantly. The points within the range on the scale that were selected by one or more of the pilots were as follows: 1-fully alert, 2-not at peak, 3-somewhat fresh, 4-a little tired, 5-moderately tired. All means fell between the values of 2 and 3. Analysis of the results from self-ratings for fatigue confirmed the indication that there were neither significant interactions nor significant main effects ( $p > .10$ ) for either the apparel (SFG versus CDE) or the dosage (PB versus placebo) factors.

Table 10. Fatigue and Workload Self-Ratings

Scale	Apparel worn during session in simulator			
	SFG		CDE	
	Self-ratings after (3x/8 hours) dosages		Self-ratings after (3x/8 hours) dosages	
	PB	Placebo	PB	Placebo
Self-ratings for fatigue				
M	2.2	2.4	2.7	2.3
SD	0.8	1.4	1.4	1.2
Range <sup>a</sup>	1 - 4	1 - 5	1 - 5	1 - 4
Self-ratings for workload				
M	3.7	3.9	4.1	4.2
SD	0.9	0.8	0.5	0.6
Range <sup>b</sup>	2 - 5	2 - 5	3 - 5	3 - 5

<sup>a</sup>Items 1 to 5: 1-fully alert; 2-not at peak; 3-somewhat fresh; 4-a little tired; 5-moderately tired.

<sup>b</sup>Items 2 to 5: 2-minimum system demands; 3-active involvement; 4-challenging but manageable; 5-barely able to keep up.

### Workload

Further inspection of Table 10 for results of self-ratings on the second of the two scales shows that estimates of workload demands extended from 2 to 5 within the 7-point scale. The steps within the range of the 7-point scale that were selected by one or more of the 24 pilots were as follows: 2-minimum system demands, 3-active involvement, 4-challenging but manageable, and 5-barely able to keep up. The statistical analysis showed that there were no significant interactions and no significant main effects ( $p > .10$ ).

## IV. DISCUSSION

The effects of PB on pilot physiology during performance of the simulated missions were directly assessed through informal interviews and questionnaires. The data obtained in these assessments were supplemented by results obtained with the Honeywell recording system. This system provided useful data for analysis of the physiological effects of wearing CDE and of taking PB. No hardware problems were encountered with this system during the experiment. Further, there was no electrical noise from the flight simulator or from other sources to contaminate the recordings.

### Symptomatology

An administration of an individual 30 mg dosage of PB to each pilot (Table 2) produced no more than mild pharmacological effects for any of the 24 pilots in the screening test. The mean values for plasma PB (ng/ml) and for ChE inhibition (%) indicated normal tolerance for the drug (Koelle, 1985). Further, there was no indication from the results shown in Table 2 that any one of the 24 pilots was unable to tolerate a 30 mg dosage of PB.

PB is readily metabolized (half-life = 2 hours approximately). Therefore, there is little buildup of the drug in the body with spaced dosages (Koelle, 1985). Presumably, the PB tolerance shown by the pilots in the screening test should have been demonstrated when three 30 mg

dosages of the drug were administered at 8-hour intervals (30 mg/ 3x/day). Nonetheless, there was evidence that some side effects resulted for half of the subjects. Table 3 shows that, despite the double-blind experimental procedure, 12 pilots reported symptoms (range, 1 to 8) from taking PB tablets whereas only 4 reported symptoms after taking the placebo.

All 12 of the pilots who reported one or more symptoms correctly guessed which series of three tablets consisted of PB and which consisted of the placebo. In addition, two pilots who reported no symptoms after taking both series of tablets correctly guessed the correct order of PB/placebo administrations. Table 4 shows, however, that the 14 pilots who correctly identified the actual orders of PB/placebo administration were no more affected by plasma PB buildup than were pilots who guessed incorrectly. Similarly, the degree of success among the pilots in guessing the order of PB/placebo administration was not associated with the extent to which PB induced ChE inactivation in the blood plasma.

### **Biobehavioral Results**

Skin temperatures (Table 9) of the 12 pilots outfitted in CDE differed significantly from those of the 12 pilots who wore SFG during the test sessions (Sessions #4 and #5). A marginal effect of CDE on the heart rate/respiratory rate ratio (Table 8) was noted. Though the ANOVA test was not significant at the conventional level ( $p = .05$ ), the observed difference was in the expected direction. On both counts, the CDE presumably placed greater stress on the pilots than did the SFG. The stressful effect of CDE on the heart rate/respiratory rates may be noted from examination of Table 8. The SFG pilots tended to match the textbook ratio of 4:1 (72 heart beats/minute to 16 respiratory cycles/minute) for the normal young adult. In contrast, the pilots who wore CDE tended toward the upper limit of the normal range, with ratios in the different tasks exceeding 5:1 in the placebo condition. Presumably, CDE would have produced greater deviations from normal heart rate/respiration rate values had this gear been worn by subjects who were not in the top physical condition that characterized the pilots who were the subjects in this study.

Furthermore, in comparisons that were made at the end of all four tasks (Task 1 through Task 4), the pilots wearing CDE exhibited significantly higher skin temperature in the dorsal neck area than did pilots wearing SFG. This effect was evident despite the fact that skin temperature in this area significantly increased for both the CDE and SFG groups during the course of the 55-minute test sessions.

There was no significant difference for between-groups effects (CDE versus SFG) on any of the other neuromuscular and physiological measures used in this study, with the exception of heart rate at the start of the session. This difference was most likely the result of the effort expended in donning the CDE.

Analysis of within-subjects effects in the study, however, showed two sets of significant effects of PB on physiological functions. Heart rates (bpm) (Table 6) and heart rate (beats/minute)/respiratory rate (rpm) ratios (Table 8) were apparently suppressed by dosages of PB (30 mg/3x/day). Examination of Table 6 suggests that there was some manner of interaction between task difficulty and the degree to which PB lowered the heart rate.

At the start of Task 1, the pilots given PB had a significantly ( $p < .05$ ) lower mean heart rate than did the pilots who had been given the placebo. At the end of Task 1, though, the within-groups effect for dosages was nonsignificant ( $p > .10$ ). Task 1 (takeoff/patterns/engine out/landing) was a relatively simple task. Inferentially, the pilots were under greater physiological

stress in adjusting to the start of the simulated mission than they were at the end of the routine activities that constituted Task 1.

Most pilots would agree that RED FLAG is more stressful than air-to-air refueling or low-angle strafe. Therefore, the finding that the mean heart rates of the 24 pilots were significantly more suppressed at the end of Task 2 (air-to-air refueling) and Task 3 (low-angle strafe) ( $p < .05$ ), but not at the end of Task 4 (RED FLAG), was interesting. Perhaps there were additional factors in the simulation of Tasks 2 and 3 which led to increased stress. The air-to-air refueling task was particularly challenging due to constraints of the visual system. The majority of the 24 pilots commented on this during data collection. On several occasions, the simulated A-10 GAU-8 gun did not work on the low-angle strafe task. On these occasions, the pilots were delayed as much as an hour or more, which caused additional stress due to the 2-hour window for drug effectiveness.

Moreover, PB may have had an effect on bpm/rpm ratios (Table 8). Just as there was an effect of gear in increasing this ratio, there was also a dosages effect ( $p < .05$ ) and a significant gear x dosages interaction. These findings may be integrated with the results shown in Table 6. From this comparison, it appears that PB tended to reduce the bpm/rpm ratios, but that wearing CDE had the compensating effect of increasing the bpm/rpm ratios over the four different tasks. In sum, there appear to have been two opposed trends. One trend was a tendency of PB dosages to lower heart rate and to bring the bpm/rpm ratio toward the normal (textbook) value of 4:1. The other trend was for wearing CDE to effect an increase in the bpm/rpm ratio above the textbook value.

The finding that PB (30 mg, 3x/day) has a suppressive effect on heart rates (bpm) is in line with other findings (Berger, 1982; Brimblecombe, 1974). Specifically, PB forms a reversible (temporary) bond with AChE and thereby liberates ACh for prolonged duration of action. One primary effect of ACh as the transmitter agent of the vagus nerve is to retard cardiac activity. In like manner, the effect of the CDE on skin temperature and in altering the bpm/rpm ratios was entirely expected.

Not all expectations, however, were confirmed. Thus, no significant effects of PB on dimensions of cardiac functions, other than heart rate, were found; and no effects were obtained for PB on respiratory activity.

The general findings of the study, however, are strongly in support of the determination by the Air Force Surgeon General that PB, in authorized dosages (30 mg, 3x/day), is safe for use by Air Force personnel as a pretreatment drug in chemical warfare defense. A caveat to that statement of strong support, nonetheless, resides in findings that occasionally individuals of European descent exhibit intolerance for PB at dosages that are readily tolerated by the great majority of normal individuals (Koelle, 1985).

## V. CONCLUSIONS

The present study was performed to determine the effects of the chemical defense pretreatment drug pyridostigmine bromide (PB) on several dimensions of pilot performance and physiology. This report deals with the evaluation of the changes occurring in pilot physiology during the study. Measurements in several biobehavioral categories were obtained from 24 USAF A-10 pilots after they had, on one occasion, orally taken a series of three PB tablets (30 mg, 3x/day) and, following the same schedule, had taken, on another occasion, three placebo tablets (30 mg, 3x/day). Results from several pencil-and-paper assessments, from neuromuscular measures, and from recordings of autonomic nervous system functions showed that PB had several significant



effects. First, PB produced a variety of nervous system changes (primarily visceral disturbances). Second, the pilots could not distinguish the series of PB administrations from the series of placebo administrations. In addition, subjective measures (self-ratings) of fatigue effects and workload effects, obtained from each pilot at the conclusion of each test session, showed no differentially adverse effect of PB on either set of self-ratings.

Within a range of biobehavioral measurements, there were no indications that PB dosages interfered with neuromuscular functions. There was, though, the predicted finding that PB dosages tended to suppress heart rate. This suppressive effect apparently acted to compensate for the effect that wearing CDE had on increasing the heart rate (beats per minute)/respiratory rate (respirations per minute) ratios above the normal (textbook) level of 4:1.

Finally, an increase in skin temperature was noted. This increase was clearly related to the CDE, but some increase due to PB was noted at the end of Task 3. The effects of CDE and PB on skin temperature did not appear to interact.

Consequently, the present results tend to support the findings of the USAF Surgeon General that, in the dosages and the regimen used in this study (30 mg, 3x/day), PB appears to be a safe pretreatment drug for personnel who have been properly screened for PB sensitivity and who may be required to conduct flight operations in environments of chemical warfare threat. The effect of PB on performance tasks will be reported in a follow-on report.

## REFERENCES

- Air Force Regulation 169-3. (1985, July 15). Use of human subjects in research, development, test, and evaluation. Washington, DC: Department of the Air Force.
- Aquilonius, S.M., Eckernas, Hartvig, P., Lindstrom, B., & Osterman, P.O. (1980). Pharmacokinetics and oral bioavailability of pyridostigmine in man. *European Journal of Clinical Pharmacology*, 18, 423-428.
- Berger, R.A. (1982). *Applied exercise physiology*. Philadelphia, PA: Lea & Febiger.
- Bernstein, J.G. (1983). *Handbook of drug therapy in psychiatry*. Bristol, England: John Wright.
- Bignami, G., Rosic, N., Michalek, H., Milosevic, M., & Gatti, G.L. (1975). Behavioral toxicology of anticholinesterase agents: Methodological, neurochemical, and neuropsychological aspects. In B. Weiss & V.G. Laties (Eds.), *Behavioral toxicology*. New York: Plenum Press.
- Brimblecombe, R.W. (1974). *Drug actions on cholinergic systems*. Baltimore, MD: University Park.
- Bruning, J.L., & Kintz, B.L. (1987). *Computational handbook of statistics* (3rd ed.). Glenview, IL: Scott, Foresman.
- Budiansky, S. (1986). Qualified approval for binary chemical weapons. *Science*, 234, 930-932.
- Calabrese, E.J. (1983). *Principles of animal extrapolation*. New York: Wiley.
- DeHart, R.M. (1987). *Aircrew testing for tolerance to pyridostigmine bromide* (letter). Bolling AFB, DC: Office of the Surgeon General, USAF.
- Driskell, J.E., & McTaggart, A. (1985). Exploratory development: Chemical, biological, and radiological defense training. Orlando, FL: Human Factors Division, Naval Training Systems Center.
- Ferguson, R.L., Cody, L.S., & Petrie, D.F. (1986, July). *Advanced visual technology system* (AFHRL-TP-85-22, AD-B103 452L). Williams AFB, AZ: Operations Training Division, Air Force Human Resources Laboratory.
- Four echelon medical care system analysis*. (1984). (F33615-82-C-0515). Brooks AFB, TX: Aerospace Medical Division.
- Fraile, R. (1984). Curbing chemical warfare. *World Press Review*, 31, 35-40.
- Graham, C., & Cook, M.R. (1984). Effects of pyridostigmine on psychomotor and visual performance (TR-84-052). Wright-Patterson AFB, OH: Air Force Aerospace Medical Research Laboratory.
- Haber, L.F. (1986). *The poisonous cloud*. New York: Clarendon (Oxford University Press).
- Harris, R., & Paxman, J. (1982). *A higher form of killing: The secret study of chemical and biological warfare*. New York: Hill and Wang.
- Koelle, G.B. (1985). *Anticholinesterase agents*. In A.G. Gilman, L.S. Goodman, T.W. Rall, & F. Murad (Eds.), *Goodman and Gilman's the pharmacological basis of therapeutics* (7th ed.). New York: Macmillan.

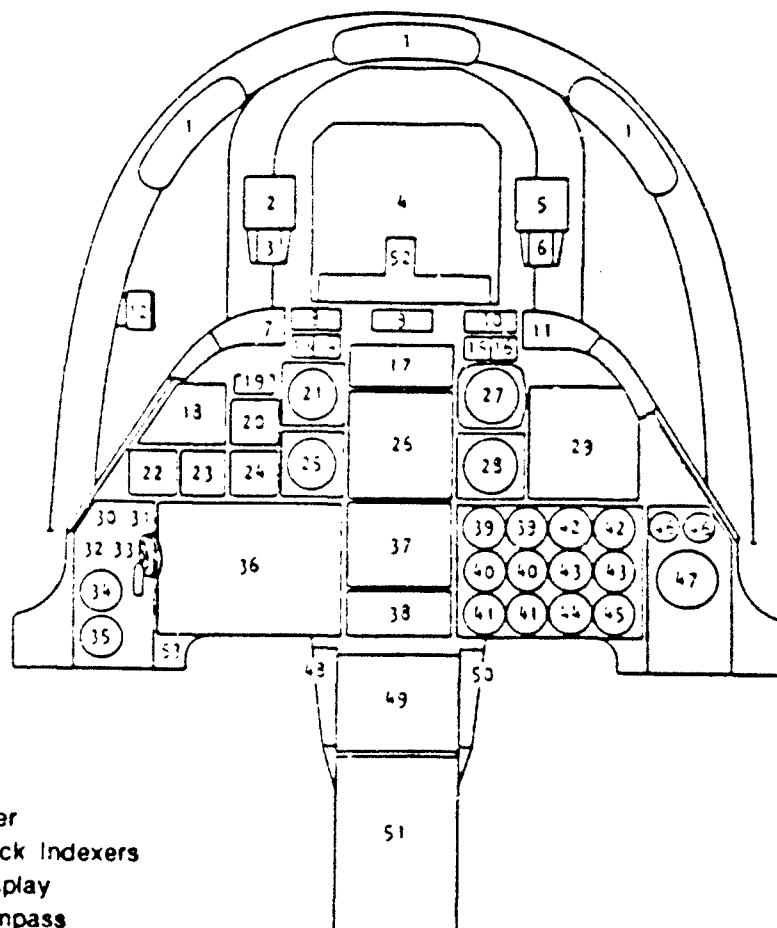
Siegel, S. (1956). *Nonparametric statistics*. New York: McGraw-Hill.

Wannarka, G.L. (1984). Status of the pyridostigmine development effort. *Fourth Annual Chemical Defense Bioscience Review*. Aberdeen Proving Ground, MD: U.S. Army Medical Research Institute of Chemical Defense.

Whinnery, J.E. (1985) Pyridostigmine bromide: A pre-exposure antidote for specific chemical warfare nerve agents: A condensed review for the aeromedical specialist (USAFSAM-TR-84-15). Brooks AFB, TX: Aerospace Medical Division.

Williams, J.I. (1984). Human response to pyridostigmine bromide (AFAMRL-TR-84-004). Wright-Patterson AFB, OH: Air Force Aerospace Medical Research Laboratory.

# APPENDIX A: A-10 OPERATIONAL INSTRUMENTS AND COCKPIT LAYOUT



2. Accelerometer
3. Angle-of-Attack Indexers
4. Head-Up Display
5. Standby Compass
13. Gun Ready Light
14. Nosewheel Steering Engaged Light
17. Radar Warning Receiver Control Indicator
19. Master Caution Light
20. Standby Altitude Indicator
21. Radar Warning Receiver Azimuth Indicator
24. Angle-of-Attack Indicator
25. Airspeed Indicator
26. Altitude Director Indicator
27. Vertical Velocity Indicator
28. Altimeter
32. Landing Gear Position Display
33. Landing Gear Handle and Override Button
34. Flap Position Indicator
37. Horizontal Situation Indicator
38. Navigation Mode Select Panel
39. Interstage Turbine Temperature Indicator (L and R)
50. Rudder Pedal Adjustment Handle

# APPENDIX B: OTHER MEASURES

## SYMPTOM CHECKLIST

DATE: \_\_\_\_\_

TIME: \_\_\_\_\_

Please circle below if any symptoms apply to you right now. If you answer YES, circle the number which best describes the degree of the symptom.

		Slight		Moderate			Severe		
1. Headache	YES	1	2	3	4	5	6	7	
2. Drowsiness	YES	1	2	3	4	5	6	7	
3. Irritability	YES	1	2	3	4	5	6	7	
4. Depression	YES	1	2	3	4	5	6	7	
5. Dizziness - eyes open	YES	1	2	3	4	5	6	7	
6. Dizziness - eyes closed	YES	1	2	3	4	5	6	7	
7. Vertigo	YES	1	2	3	4	5	6	7	
8. Confusion	YES	1	2	3	4	5	6	7	
9. Giddiness/euphoria	YES	1	2	3	4	5	6	7	
10. Faintness	YES	1	2	3	4	5	6	7	
11. Fatigue	YES	1	2	3	4	5	6	7	
12. Boredom	YES	1	2	3	4	5	6	7	
13. Inability to think	YES	1	2	3	4	5	6	7	
14. Numbness	YES	1	2	3	4	5	6	7	
15. Tingling	YES	1	2	3	4	5	6	7	
16. Hot/cold flashes	YES	1	2	3	4	5	6	7	
17. Awareness of breathing	YES	1	2	3	4	5	6	7	
18. Rapid breathing	YES	1	2	3	4	5	6	7	
19. Irregular breathing	YES	1	2	3	4	5	6	7	
20. Chest pain	YES	1	2	3	4	5	6	7	
21. Difficulty breathing	YES	1	2	3	4	5	6	7	
22. Rapid heartbeat	YES	1	2	3	4	5	6	7	
23. Pounding heartbeat	YES	1	2	3	4	5	6	7	
24. Irregular heartbeat	YES	1	2	3	4	5	6	7	
25. Eyestrain	YES	1	2	3	4	5	6	7	
26. Difficulty focusing	YES	1	2	3	4	5	6	7	
27. Blurred vision	YES	1	2	3	4	5	6	7	
28. Visual illusions	YES	1	2	3	4	5	6	7	
29. Tearing	YES	1	2	3	4	5	6	7	
30. Nausea	YES	1	2	3	4	5	6	7	
31. Bellyache	YES	1	2	3	4	5	6	7	
32. Stomach discomfort (awareness)	YES	1	2	3	4	5	6	7	
33. Loss of appetite	YES	1	2	3	4	5	6	7	

34. Increased appetite	YES	1	2	3	4	5	6	7
35. Sweating	YES	1	2	3	4	5	6	7
36. Burping	YES	1	2	3	4	5	6	7
37. Vomiting	YES	1	2	3	4	5	6	7
38. Increased gas	YES	1	2	3	4	5	6	7
39. Wanting to move bowels	YES	1	2	3	4	5	6	7
40. Diarrhea	YES	1	2	3	4	5	6	7
41. Salivation increased	YES	1	2	3	4	5	6	7
42. Salivation decreased	YES	1	2	3	4	5	6	7
43. Dry mouth	YES	1	2	3	4	5	6	7
44. Thirst	YES	1	2	3	4	5	6	7
45. Muscle cramping	YES	1	2	3	4	5	6	7
46. Muscle twitching	YES	1	2	3	4	5	6	7
47. Muscle weakness	YES	1	2	3	4	5	6	7
48. Muscle incoordination	YES	1	2	3	4	5	6	7
49. Muscle fatigue	YES	1	2	3	4	5	6	7
50. Nosebleed	YES	1	2	3	4	5	6	7
51. Shortness of breath	YES	1	2	3	4	5	6	7
52. Ringing in ears	YES	1	2	3	4	5	6	7
53. Itching	YES	1	2	3	4	5	6	7
54. Chills/shaking	YES	1	2	3	4	5	6	7
55. Other symptoms?	YES	1	2	3	4	5	6	7
List 55.	YES	1	2	3	4	5	6	7
56.	YES	1	2	3	4	5	6	7
57.	YES	1	2	3	4	5	6	7
58.	YES	1	2	3	4	5	6	7
59.	YES	1	2	3	4	5	6	7

CAFFEINE/TOBACCO QUESTIONNAIRE

PILOT \_\_\_\_\_  
NUMBER \_\_\_\_\_

DATE \_\_\_\_\_

ABOUT HOW MANY HOURS OF SLEEP DID YOU HAVE LAST NIGHT? \_\_\_\_\_

HAVE YOU HAD ANY ALCOHOLIC BEVERAGES IN THE PAST 24 HRS? \_\_\_\_\_  
IF SO, WHEN? \_\_\_\_\_ HOW MUCH? \_\_\_\_\_

HAVE YOU HAD ANY CAFFEINATED BEVERAGES IN THE PAST 8 HRS? \_\_\_\_\_

COFFEE: \_\_\_\_\_ HOW MUCH? \_\_\_\_\_

TEA: \_\_\_\_\_ HOW MUCH? \_\_\_\_\_

SOFT DRINKS: \_\_\_\_\_ HOW MUCH? \_\_\_\_\_

OTHER: \_\_\_\_\_ HOW MUCH? \_\_\_\_\_

HOW MANY CIGARETTES HAVE YOU SMOKED IN THE PAST 8 HRS? \_\_\_\_\_

HAVE YOU EATEN A MEAL IN THE PAST TWO (2) HOURS? \_\_\_\_\_

IF SO, PLEASE LIST ITEMS ON BACK OF THIS SHEET. \_\_\_\_\_

ARE YOU CURRENTLY TAKING ANY MEDICATION? \_\_\_\_\_

IF SO, PLEASE LIST THE DRUG(S) YOU ARE TAKING. \_\_\_\_\_

(Answer questions below only first time questionnaire is given)

DO YOU WEAR CORRECTIVE LENSES? \_\_\_\_\_

TOTAL HOURS OF MILITARY FLYING TIME? \_\_\_\_\_

FLIGHT HOURS IN THE A-10? \_\_\_\_\_

NUMBER OF RED FLAG/MAPLE FLAG-TYPE EXERCISES. \_\_\_\_\_

WHAT FIGHTERS HAVE YOU FLOWN IN ADDITION TO THE A-10? \_\_\_\_\_

HOURS IN SIMULATOR IN PAST YEAR? \_\_\_\_\_

## APPENDIX C: SCENARIOS

The following tasks were performed in the simulator: (1) Takeoff, pattern work, engine out; (2) aerial refueling; (3) strafe; and (4) low-level ingress, RED FLAG. Each pilot was briefed as follows for each of the four tasks.

### Task 1: Takeoff, Pattern Work, Engine Out (15 min)

#### a. First Pattern

The initial condition is on Runway 3 at Nellis AFB, Nevada, at a dead stop. The field elevation is 1,868 feet Mean Sea Level (MSL). You will be under visual flight rules (VFR). Tactical Air Navigation (TACAN) is not available. You will have the Instrument Landing System (ILS) course and glideslope to help you on final as desired. Make your normal takeoff and accelerate to 250 knots. At 2,900 feet MSL, start a left turn to a heading of 300 for a crosswind leg and level-off at 4,000 feet MSL. Shortly after establishing the crosswind, you will see two fairly thick parallel white lines angling in front of you. They represent a large powerline right-of-way. Turn to a heading of 210 for a downwind just before crossing the powerlines. Within 30 seconds after rolling out on downwind, you will see a green area in front of you and to the right that represents a golf course. It is the primary reference for your downwind track. Fly slightly to the left of it. Continue on past the golf course about 1 more minute and you will see a black line angling across in front of you. This represents a major road. Turn to base just before you cross it. You will see some figures which represent Las Vegas hotels in the distance (the closer, left-hand group). Aim just to the right of them on your base heading of 120°. Turn to final, heading 030, shortly after you fly past the hotels or use the Course Deviation Indicator (CDI) to make a course intercept on the 028 radial. Once you roll out, you will soon be able to see two small red lights in the distance. These are at the near end of the runway. Aim for the one on the left if you see them. This should put you on a 7-nautical-mile final. You will fly over a large green area on final about 5 nautical miles out. Check to see that your gear is down. Proceed visually once you pick up the runway/base environment and do a touch-and-go.

#### b. Second Pattern

Do the same thing you did last time, except this time you can expect to experience an engine problem in the area of the golf course downwind. Handle the problem as you normally would. Check to see that the following switches are off: Auxillary Power Unit (APU) generator, APU start, and crossfeed. Be sure the Stability Augmentation System (SAS) is on. Check to see that the gear is down. Fly the remainder of the pattern to a full-stop landing using whatever techniques you would expect to use in the real world.

### Task 2: Aerial Refueling (8 min)

The initial condition is 1,000 feet behind the tanker, which is at an altitude of 16,000 feet and moving at approximately 200 knots. The probe is in the nose. The objective is to hook up and take as much fuel as possible.

### Task 3: Conventional Low-Angle Strafe (LAS) (12 min)

The target that you will be shooting at will be the leftmost target in the right-hand pit. Squeeze the trigger and watch to make sure the rounds impact the center of the target. For the conventional strafe runs, you will be initialized on a base leg at 5,500 feet MSL, heading



approximately 080 degrees, at 300 knots to do a left-hand pattern. The target areas or strafe pits will be in your left ten-o'clock position and show up as two fairly large rectangular areas that are darker colored than the surrounding terrain. You have unlimited rounds. Your goal is to get the highest percentage (not just hits) in the 12 minutes allotted. You will be given feedback on the total percent for that pass only.

**Task 4: Low-Level Ingress/RED FLAG (20 min)**

In the RED FLAG segment, you have no chaff, flares or Electronic Countermeasures (ECM). Your only weapon is the gun. You have unlimited bullets. This is a model of the real-world Nellis range. Terrain elevation at the start point is approximately 5,400 feet MSL. As you fly the low-level, try to maintain an altitude of 50-500 feet Above Ground Level (AGL). Observe that the bearing pointer is aligned with heading. It points to the steer point and updates to the next steer point automatically as each is overflown until the command post is reached. Then, it will point to the command post. There is no distance-to-steer-point readout available. The route has been planned for 350 knots. You need to do a system test on the Radar Warning Receiver (RWR) prior to entering the target area. For leg one, the heading is 248° for 20 nm. For leg two, the heading is 197° for 15.5 nm. For leg three, the heading is 260° for 14 nm. From the Initial Point (IP), the heading is 220° for 8 nm. The targets are located in the smaller, northernmost salt flats in the Kawich Valley between Belted Peak and Quartzite Mountain. The target area elevation is approximately 5,300 feet. Additional targets include the following:

- a. Kawich Airfield. Located about 180° south of command post (approximately 7 nm).
- b. Airborne Regiment. Located about 90° east of command post (approximately 1.5 nm).
- c. Industrial Complex. Located southeast of Kawich Airfield. Target is downstairs center of northeast building.
- d. Both SA-4 sites.

# APPENDIX D: PERFORMANCE MEASURES

## RAW SIMULATOR DATA RECORDED DURING TASK ONE CHEMICAL WARFARE DEFENSE STUDY

Task One: Fifteen (15) minutes duration. Take off from Nellis AFB, fly a prescribed flight pattern at 4,000 feet MSL, perform a touch-and-go at Nellis AFB, repeat the pattern, and experience a mid-air engine failure and then perform a single-engine landing at Nellis AFB.

<u>WORD</u>	<u>DATAPOOL NAME</u>	<u>TYPE</u>	<u>PARAMETER DESCRIPTION</u>
1	WNALATDP	ED	A/C LATITUDE (FIRST WORD)
2			" (SECOND WORD)
3	WNALONDP	ED	A/C LONGITUDE (FIRST WORD)
4			" (SECOND WORD)
5	AFHGEO	EW	A/C ALTITUDE
6	AFUE	EW	A/C X VELOCITY (EARTH)
7	AFVE	EW	A/C Y VELOCITY (EARTH)
8	AFWE	EW	A/C Z VELOCITY (EARTH)
9	AFDUE	EW	A/C X ACCELERATION (EARTH)
10	AFDVE	EW	A/C Y ACCELERATION (EARTH)
11	AFDWE	EW	A/C Z ACCELERATION (EARTH)
12	AFGTHETA	EW	A/C PITCH ANGLE
13	AFGPHI	EW	A/C ROLL ANGLE
14	AFGPSI	EW	A/C YAW ANGLE (HEADING WRT TRUE NORTH)
15	BSCORE22	IW	MISSION ELAPSED TIME (FRAME COUNTER)
16	AFELESTK	EW	PITCH STICK
17	AFAILSTK	EW	ROLL STICK
18	AFRUDEP	EW	RUDDER
19	ADTHRL	EW	LEFT THROTTLE
20	ADTHRR	EW	RIGHT THROTTLE
21	RVR	PH	VISIBILITY (PACKED: RVR;IH + FVR;IH)
22	EFWONWSW	PB	WEIGHT ON WHEELS (PACKED:N,M,L,R IN & CONSECUTIVE BYTES)
23	AVXIMM1	ED	C-130 LATITUDE (FIRST WORD)
24	AVYIMM1		" (SECOND WORD)
25	AVO1MM1	ED	C-130 LONGITUDE (FIRST WORD)
26	AVO2MM1		" (SECOND WORD)
27	AVZ1MM1	EW	C-130 ALTITUDE
28	AVTHEMM1	EW	C-130 PITCH
29	AVPHIMM1	EW	C-130 ROLL
30	AVPSIMM1	EW	C-130 YAW
31	AV03MM1	EW	C-130 VELOCITY
32		PB	L. ENG FAIL/R. ENG FAIL/MANUAL REV (PACKED: EEMFFOL;LB + EEMFFOR;LB + EFFCNORM;LB)
33	AFV:	EW	INDICATED AIRSPEED
34		PB	APU STRT/CROSS FEED/APU GEN/SAS YAW(PACKED: EFAPUSTR + EFCSRSED + EFAPUGEN + EFYSASR)

RAW SIMULATOR DATA RECORDED DURING TASK TWO  
CHEMICAL WARFARE DEFENSE STUDY

Task Two: Eight (8) minutes duration. Initialized in the air behind a KC-135 tanker, with the objective to perform a refueling operation, taking on fuel for as long as possible in this task period.

WORD	DATAPOOL NAME	TYPE	PARAMETER DESCRIPTION
1	WNALATDP	ED	A/C LATITUDE (FIRST WORD)
2			" (SECOND WORD)
3	WNALONDP	ED	A/C LONGITUDE (FIRST WORD)
4			" (SECOND WORD)
5	AFHGEO	EW	A/C ALTITUDE
6	AFUE	EW	A/C X VELOCITY (EARTH)
7	AFVE	EW	A/C Y VELOCITY (EARTH)
8	AFWE	EW	A/C Z VELOCITY (EARTH)
9	AFDUE	EW	A/C X ACCELERATION (EARTH)
10	AFDVE	EW	A/C Y ACCELERATION (EARTH)
11	AFDWE	EW	A/C Z ACCELERATION (EARTH)
12	AFGTHETA	EW	A/C PITCH ANGLE
13	AFGPHI	EW	A/C ROLL ANGLE
14	AFGPSI	EW	A/C YAW ANGLE (HEADING WRT TRUE NORTH)
15	BSCORE22	IW	MISSION ELAPSED TIME (FRAME COUNTER)
16	AFELESTK	EW	PITCH STICK
17	AFAILSTK	EW	ROLL STICK
18	AFRUDPED	EW	RUDDER
19	ADTHRL	EW	LEFT THROTTLE
20	ADTHRR	EW	RIGHT THROTTLE
21	RVR	PH	VISIBILITY (PACKED: RVR;IH + FVR;IH)
22	AVXIMM2	ED	TANKER LATITUDE (FIRST WORD)
23	AVYIMM2		" (SECOND WORD)
24	AVO1MM2	ED	" LONGITUDE (FIRST WORD)
25	V02MM2		" " (SECOND WORD)
26	AVZIMM2	EW	"ALTITUDE
27	AVTHEMM2	EW	"PITCH
28	AVPHIMM2	EW	"ROLL
29	AVPSIMM2	EW	"YAW
30	AVO3MM2	EW	"VELOCITY
31	AVXIMM3	ED	BOOM HINGE LATITUDE (FIRST WORD)
32	AVYIMM3		" (SECOND WORD)
33	AVO1MM3	ED	"LONGITUDE (FIRST WORD)
34	AV02MM3		" " (SECOND WORD)
35	AVZIMM3	EW	" ALTITUDE
36	AVTHEMM3	EW	" PITCH
37	AVPSIMM3	EW	" YAW
38	AFXGOAL	EW	RECEPTACLE TO BOOM TIP AFT SEPARATION
39	AFYGOAL	EW	" LATERAL SEPARATION
40	AFZGOAL	EW	" VERTICAL SEPARATION

RAW SIMULATOR DATA RECORDED DURING TASK THREE  
CHEMICAL WARFARE DEFENSE STUDY

Task Three: Twelve (12) minutes duration. Initialized on a gunnery range at an altitude of 5,500 ft MSL, with the objective to perform conventional strafing runs on a conventional target panel on the ground.

WORD	DATAPool NAME	TYPE	PARAMETER DESCRIPTION
1	WNALATDP	ED	A/C LATITUDE (FIRST WORD)
2			" (SECOND WORD)
3	WNALONDP	ED	A/C LONGITUDE (FIRST WORD)
4			" (SECOND WORD)
5	AFHGEO	EW	A/C ALTITUDE
6	AFUE	EW	A/C X VELOCITY (EARTH)
7	AFVE	EW	A/C Y VELOCITY (EARTH)
8	AFWE	EW	A/C Z VELOCITY (EARTH)
9	AFDUE	EW	A/C X ACCELERATION (EARTH)
10	AFDVE	EW	A/C Y ACCELERATION (EARTH)
11	AFDWE	EW	A/C Z ACCELERATION (EARTH)
12	AFGTHETA	EW	A/C PITCH ANGLE
13	AFGPHI	EW	A/C ROLL ANGLE
14	AFGPSI	EW	A/C YAW ANGLE (HEADING WRT TRUE NORTH)
15	BSCORE22	IW	MISSION ELAPSED TIME (FRAME COUNTER)
16	AFELESTK	EW	PITCH STICK
17	AFAILSTK	EW	ROLL STICK
18	AFRUDPED	EW	RUDDER
19	ADTHRL	EW	LEFT THROTTLE
20	ADTHRR	EW	RIGHT THROTTLE
21	RVR	PH	VISIBILITY (PACKED: RVR;IH + FVR;IH)
22		PB	FIRE RATE SWITCHES/TRIGGER (PACKED: EWGRHI;LB + EWGRLO;LB + EWTRIGER;LB)
23	AFNORND5	EW	ROUNDS REMAINING
24	HUDDEPR	IW	HUD DEPRESSION
25	TERRNHGT	EW	TERRAIN HEIGHT ABOVE SEA LEVEL (DIRECTLY BENEATH OWNSHIP)
26	AFVI	EW	INDICATED AIRSPEED
27	AF30	ED	IMPACT DATA LATITUDE (WORD 1)
28	AF31		" " " (WORD 2)
29	AF32	ED	IMPACT DATA LONGITUDE (WORD 1)
30	AF33		" " " (WORD 2)
31	AF34	EW	IMPACT DATA ALTITUDE
32	AF35	IW	NUMBER AVERAGED FOR 10 HERTZ
33	AF36	PB	(4 BYTES) BUCKETS HIT IN 10 HERTZ
34	AF37	PB	" " " " " "
35	AF38	IW	TOTAL NUMBER OF ROUNDS PER PASS
36	BARBOTOT	IW	NUMBER OF ROUNDS PER BURST

# RAW SIMULATOR DATA RECORDED DURING TASK FOUR CHEMICAL WARFARE DEFENSE STUDY

Task Four: Twenty (20) minutes duration. Perform low-level navigation tasks for ingress to the Red Flag threat area and then warfare tactics tasks, in the Red Flag threat area, between the A-10 aircraft simulator and the various simulated threats and targets.

WORD	DATAPOOL NAME	TYPE	PARAMETER DESCRIPTION
1	WNLATDP	ED	A/C LATITUDE (FIRST WORD)
2			" (SECOND WORD)
3	WNALONDP	ED	A/C LONGITUDE (FIRST WORD)
4			" (SECOND WORD)
5	AFHGEO	EW	A/C ALTITUDE
6	AFUE	EW	A/C X VELOCITY (EARTH)
7	AFVE	EW	A/C Y VELOCITY (EARTH)
8	AFWE	EW	A/C Z VELOCITY (EARTH)
9	AFDUE	EW	A/C X ACCELERATION (EARTH)
10	AFDVE	EW	A/C Y ACCELERATION (EARTH)
11	AFDWE	EW	A/C Z ACCELERATION (EARTH)
12	AFGTHETA	EW	A/C PITCH ANGLE
13	AFGPHI	EW	A/C ROLL ANGLE
14	AFGPSI	EW	A/C YAW ANGLE (HEADING WRT TRUE NORTH)
15	BSCORE22	IW	MISSION ELAPSED TIME (FRAME COUNTER)
16	AFELESTK	EW	PITCH STICK
17	AFAILSTK	EW	ROLL STICK
18	AFRUDPED	EW	RUDDER
19	ADTHRL	EW	LEFT THROTTLE
20	ADTHRR	EW	RIGHT THROTTLE
21	RVR	PH	VISIBILITY (PACKED: FVR;IH + FVR;IH)
22		PB	FIRE RATE SWITCHES/TRIGGER (PACKED: EWGRHI;LB + EWGRLO;LB + EWTRIGGER;LB)
23	AFNORNDS	EW	ROUNDS REMAINING
24	HUDDEPR	IW	HUD DEPRESSION
25	TERRNHGT	EW	TERRAIN HEIGHT ABOVE SEA LEVEL (DIRECTLY BENEATH OWNERSHIP)
26	AFVI	EW	INDICATED AIRSPEED
27	BSCORE16	PB	AAA STATUS (PACKED: AAA1;IB + AAA2;IB + AAA3;IB + AAA4;IB)
28	BSCORE24	PB	AAA STATUS (PACKED: AAA5;IB + AAA6;IB + # OWNERSHIP KILLED;IB + NOT USED;IB)
29	BSCORE17	PB	SAM STATUS (PACKED: SAM1;IB + SAM2;IB + SAM3;IB + SAM4;IB)
30	BSCORE18	PB	SAM STATUS (PACKED: SAM5;IB + SAM6;IB + SAM7;IB + SAM8;IB)
31	BSCORE19	IW	# OF OWNERSHIP KILLS BY SAMS
32	BSCORE15	IW	# OF TARGETS KILLED BY OWNERSHIP
33	BSCORE21	IW	MODEL ID OF THE TARGET KILLED
34	BARNDTOT	IW	NUMBER OF ROUNDS PER BURST

## APPENDIX E: ACRONYMS AND ABBREVIATIONS

AAA	Anti-Aircraft Artillery
AAR	Air-to-Air Refueling
ACh	Acetylcholine
AChE	Acetylcholinesterase
AEF	American Expeditionary Force
AFB	Air Force Base
AFHRL/OT	Air Force Human Resources Laboratory/ Operations Training Division
AGL	Above Ground Level
APU	Auxiliary Power Unit
AVTS	Advanced Visual Technology System
BPM	(Heart) Beats Per Minute
C	Celsius
CBR	Chemical, Biological, Radiation
CDE	Chemical Defense Ensemble
CDI	Course Deviation Indicator
CIG	Computer Image Generator
cm	Centimeter
cm/sec	Centimeters per second
CW	Chemical Warfare
DMA	Defense Mapping Agency
DoD	Department of Defense
ECG	Electrocardiogram
ECM	Electronic Countermeasures
EMG	Electromyogram
FDA	Food and Drug Administration
GD	Soman
HSD	High-Speed Data
Hz	Hertz
ILS	Instrument Landing System
IOS	Instructor/Operator Station
IP	Initial point
JWGD <sup>3</sup> MIL.PERF	Joint Working Group on Drug Dependent Degradation of Military Performance
Kg	Kilogram

L	Left
LAS	Low-Angle Strafe
<u>M</u>	Mean
MG	Myasthenia Gravis
ml	Milliliters
mm	Millimeters
MSL	Mean Sea Level
NATO	North Atlantic Treaty Organization
ng/ml	Nanograms per milliliter
<u>p</u>	Probability
PB	Pyridostigmine Bromide
PICS	Programmable Interface and Collection System
QRS	The three primary electrical components of the heartbeat are: the Q wave (the first downward stroke), R wave (the upward deflection), and the S wave (the downstroke following the R wave)
<u>r</u>	Pearson product moment correlation
R	Right
RPM	Respirations Per Minute
R waves	See QRS complex
RWR	Radar Warning Receiver
SAM	Surface-to-Air Missile
SD	Standard Deviation
SEM	Standard Error of the Mean
SFG	Standard Flight Gear
TACAN	Tactical Air Navigation
TFW	Tactical Fighter Wing
U/L	Units per liter
US	United States
USAF	United States Air Force
USSR	Union of Soviet Socialist Republics
VAX	Label for a Digital Corporation Mainframe Computer
VFR	Visual Flight Rules
$\chi^2$	Chi square
<u>z</u>	Standard score